Office Action Summary	Application No.	Applicant(s)	
	09/889,203	BROWN, TRACEY	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date. _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for continued examination filed under 37 CFR 1.114, amendment and remarks, 10/30/07. Claims 10-26 are canceled. New claims 27-52 are added and are pending.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 27-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

5. New claims 27, 33, 38, 39, 44 and 50 seek to exclude polynucleic acid based cytotoxic agent, but the original specification has not envisioned excluding or including polynucleic acid basted cytotoxic agents.

6. Claims 27-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 27 and 33 recite the limitation "the efficacy" in 1. There is insufficient antecedent basis for this limitation in the claim. The recitation of "the efficacy" in claims 27 and 33 is the first occurrence and does lack antecedence in the claims

Response to Arguments

8. Applicant's arguments filed 10/31/07 have been fully considered but they are not persuasive.

Applicant states that the examiner did not raise any issue with the limitation when it was first introduced on 10/28/2005 and the negative limitation is added according to In re Johnson at 558 F.2d 1008, 1019, 194 USPQ 187, 186 (CCPA 1977 and that the negative limitation is fully supported by the original specification.

9. The negative limitation, adding new matter to the claims was inadvertently missed in the office action of 3/10/2006. When limitations or subject matter that do not derive antecedence from the original specification is rejected under new matter. The In re Johnson case does not remove the new matter form the claims.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 27, 28, 32-34, 38-40, 44-46 and 50 are rejected under 35 U.S.C. 102(e) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Falk et al. (US 5,985,850).

Falk discloses injectable formulations comprising anti-cancer agent or chemotherapeutic agent and hyaluronic acid (column 10, lines 8-59). The preferred molecular weight for the hyaluronan is less than 750,000 Daltons (claims 142, 83, 84 and 92). The anti-cancer drug or chemotherapeutic agent of Falk, specifically, methotrexate and 5-fluorouracil (claims 38 and 79) meet the drug and/or anti-neoplastic agent requirement of claims 10, 11, 15 and 16. The method of administration of the hyaluronan containing composition is by intravenous, intra arterially, intraperitoneally, intrapleurally, transdermally, topically, rectally, or by direct injection of the of the composition into a tumor (column 10, lines 48-55) and this administration meets the requirements of the method claims where the method step administers the composition. Since the

method of claim 27 administers the hyaluronan and drug composition to a patient to enhance the efficacy of a drug for a cancer cell, it flows that, when Falk administers the same composition to tumor site of a patient, the composition would inherently enhance the efficacy of the drug for cancer cell. Applicant's declaration, as previously noted, is not commensurate with 750 kDa. Thus, the demonstration provided in applicant's declaration has no data at the lower end of 750 kDa and the 30 kDa data is much lower than 750 kDa. Therefore, there is no conclusive factual evidence that molecular weight equal to 750,000 Dalton provides unusual and unexpected results. Therefore, the evidence provided does not support hyaluronic acid having molecular weight of equal to 750,000 Daltons as being inventive over the disclosure in the prior art of a molecular weight of less than 750,000. Falk anticipates the claims. However, in the, alternate, since Falk does not explicitly state that efficacy of a drug for a cancer cell is enhanced by administering a composition containing hyaluronan and anti-neoplastic agent or cytotoxic agent, it would be expected that the administration of the composition containing hyaluronan and anti-neoplastic agent or cytotoxic agent to a patient as described by Falk would provide the effect recited in the claims thereby rendering obvious the effect of enhancing the efficacy of a drug for cancer cell. It is noted that a range of molecular weight is recited indicating that one can use the hyaluronic acid having an optimum molecular weight for the desired goal. Furthermore, a molecular weight of recited molecular weight range at the lower limit of 400,000 Da is less than 750,000 Da so that the less than 750,000 Da for the HA meets the requirements of the claims.

Response to Arguments

12. Applicant's arguments filed 10/31/07 as it relates to the current rejection have been fully considered but they are not persuasive.

Applicant argues that Falk does not teach every limitation of the claimed invention because, Falk does not explicitly state that the efficacy of a cancer drug is enhanced by administering a composition containing hyaluronic acid and cytotoxic agent and does not teach the claimed molecular weight range for the HA.

13. **Response**:

14. In response to applicant's argument stated above, it is noted that Falk teaches all the limitations of the claimed invention of claims 27, 28, 32-34, 38-40, 44-46 and 50 because, the claims are directed to a HA having a molecular weight in the range of 400,000 to 900,000 Da and the lower limit of 400,000 is less than 750,000 Da.; secondly, Falk administers composition comprising HA and antineoplastic agent that meets the claimed method step for enhancing the efficacy of the antineoplastic agent, which is administration of the composition containing HA and the antineoplastic agent. Since the method of claim 27 administers the hyaluronan and drug composition to a patient to enhance the efficacy of a drug for a cancer cell, it flows that, when Falk administers the same composition to tumor site of a patient, the composition would inherently enhance the efficacy of the drug for cancer cell.

15. Claims 27, 28, 32-34, 38-40, 44-46 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by della Valle et al. (US 5,442,053).

16. della Valle describes an embodiment in which a pharmaceutical composition comprising active agents and hyaluronic acid as the carrier vehicle (abstract) for administration in various forms (column 3, lines 60 and 61; column 5, line 60; column 14, line 13; column 16, lines 38-46; column17, line 11). The cytotoxic agents named in della Valle are fluorouracil, methotrexate and podophyllin (column 24, lines 65 and 66) meeting the requirements of claims 27, 32, 33, 38, 44 and 50. Hyaluronic acid having molecular weight of from between 300,000 and 730,000 Da is

used (claims 5, 8, 18 and 32) meeting the requirements of claims 27, 28, 33, 34 and 40. The administering of the composition comprising the HA and the cytotoxic agents meets the administration limitation of the method steps of the claims.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 27, 29-31, 35-38, 41-43, 47-49, 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over della Valle et al. (US 5,442,053).

19. della Valle is discussed above. della Valle does not use hyaluronic acid having molecular weight of claims 29-31, 35-37, 41- 43, 47-49, 51 and 53. However, the disclosure to use hyaluronic having a range of molecular weight or from about 500,00 to about 730,000 Da (claims 5, 8, 18 and 32), and the general teaching that as a vehicle, hyaluronic acid of varying molecular weights can be used (column 18, lines 63-66), suggest that although, molecular weight in the range of about 500,000 to 730,000 Da may be used, hyaluronic acid of other molecular weight may also be used including hyaluronic acid of molecular weight higher than 730,000 Da being mindful of the intrinsic viscosity of the hyaluronic acid carrier vehicle (column 4, lines 13-23). Therefore, taking the general teaching of della Valle, the person of ordinary skill in the art at the

time the invention was made would have reasonable expectation of success that using hyaluronic acid having molecular weights in a range that is higher than the 730,000 Da that results in a carrier vehicle having desired viscosity would provide the anticipated therapeutic composition for successful delivery of cytotoxic agents..

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 7571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Blessing M. Fubara/
Examiner, Art Unit 1618